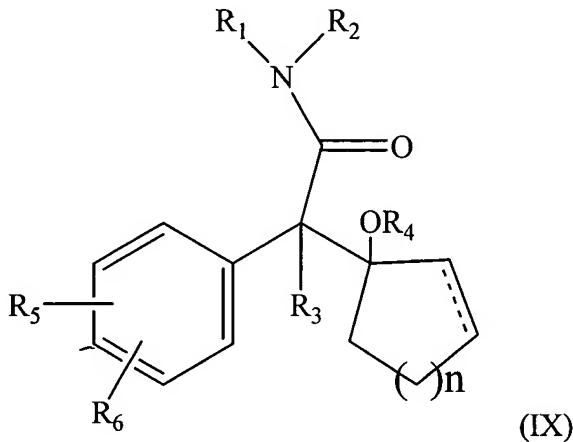


We claim:

1. A pharmaceutical preparation comprising a nefazodonoid and a serotonin reuptake inhibitor (SRI), in a pharmaceutically acceptable excipient. P.2D *written in*
2. The preparation of claim 1, wherein the nefazodonoid is selected from nefazodone, hydroxynefazodone, oxonefazodone, a mixture thereof, and pharmaceutically acceptable salts thereof.
 3. The preparation of claim 1, wherein the nefazodonoid is R-hydroxynefazodone.
 4. The preparation of claim 1, wherein the SRI is a compound represented in Formula (IX), or a pharmaceutically acceptable salts thereof:



wherein

R_1 is hydrogen or alkyl of 1 to 6 carbon atoms;

R_2 is alkyl of 1 to 6 carbon atoms;

R_3 is hydrogen or alkyl of 1 to 6 carbon atoms;

R_4 is hydrogen, alkyl of 1 to 6 carbon atoms, formyl, or alkanoyl of 2 to 7 carbon atoms;

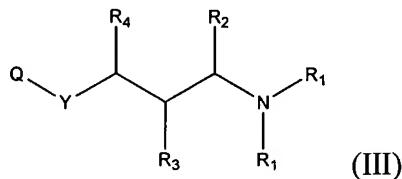
R_5 and R_6 are independently hydrogen, hydroxyl, alkyl of 1 to 6 carbon atoms,

alkoxy of 1 to 6 carbon atoms, alkanoyloxy of 2 to 7 carbon atoms, cyano, nitro, alkylmercapto of 1 to 6 carbon atoms, amino, alkylamino of 1 to 6 carbon atoms, dialkylamino in which each alkyl group is of 1 to 6 carbon atoms,

alkanamido of 2 to 7 carbon atoms, halo, trifluoromethyl, or, when taken together, methylene dioxy; and

n is one of the integers 0, 1, 2, 3 or 4.

5. The preparation of claim 1, wherein the SRI is a selective serotonin reuptake inhibitor (SSRI).
6. The preparation of claim 5, wherein the SSRI is a fluoxetinoid.
7. The preparation of claim 5, wherein the SSRI is a compound having a structure represented in formula (III), or a pharmaceutically acceptable salts thereof:



wherein, as valence and stability permit,

2W

R₁, independently for each occurrence, represents H or lower alkyl, preferably H or Me;

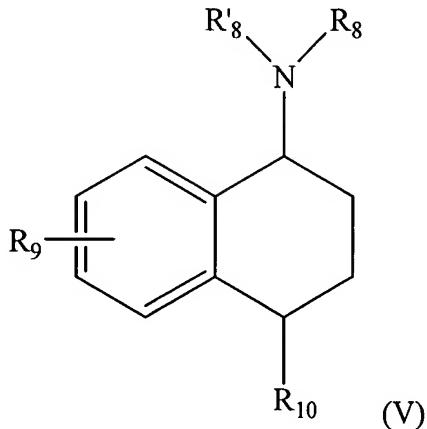
R₂, R₃, and R₄ each independently represent H, methyl, substituted or unsubstituted phenyl, or substituted or unsubstituted phenylmethyl, such that exactly one of R₂, R₃, and R₄ is a substituted or unsubstituted phenyl, or substituted or unsubstituted phenylmethyl;

Y represents O, S, or -S(O)₂, preferably O;

Q represents a substituted or unsubstituted aryl or heteroaryl ring.

8. The preparation of claim 6, wherein the fluoxetinoid is selected from fluoxetine and norfluoxetine, a mixture thereof, and pharmaceutically acceptable salts thereof.
9. The preparation of claim 8, wherein the SSRI is R-fluoxetine.

10. The preparation of claim 5, wherein the SSRI is a compound having a structure represented in formula (V), or a pharmaceutically acceptable salts thereof:

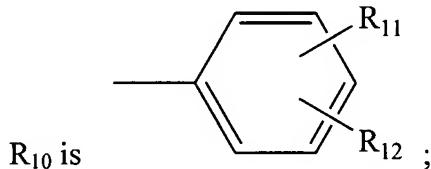


wherein

R_8 is selected from the group consisting of hydrogen and normal alkyl of from 1 to 3 carbon atoms;

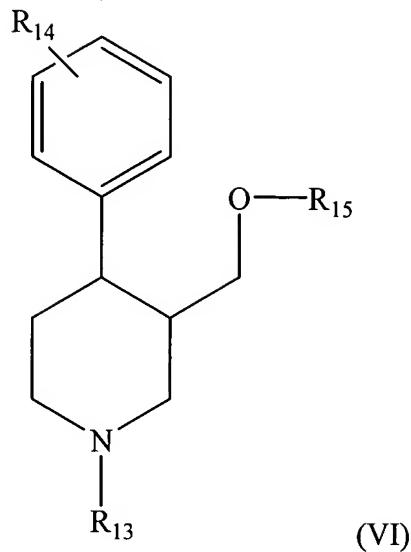
R'_8 is normal alkyl of from 1 to 3 carbon atoms;

R_9 is selected from the group consisting of hydrogen, fluoro, chloro, bromo, trifluoromethyl and alkoxy of from 1 to 3 carbon atoms;



R_{11} and R_{12} are each independently selected from the group consisting of hydrogen, fluoro, chloro, bromo, trifluoromethyl, alkoxy of from 1 to 3 carbon atoms and cyano, with at least one of R_{11} and R_{12} being other than hydrogen.

11. The preparation of claim 5, wherein the SSRI is a compound having a structure represented in formula (VI), or a pharmaceutically acceptable salts thereof:



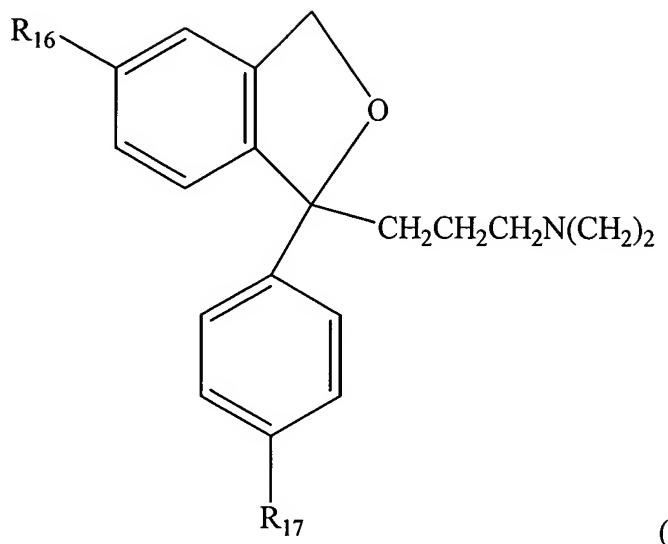
wherein

R_{13} represents hydrogen or an alkyl group of 1-4 carbon atoms, and

R_{14} represents hydrogen, alkyl having 1-4 carbon atoms, C1-6 alkoxy, C1-6 trifluoroalkyl (preferably, trifluoromethyl), hydroxy, halogen, methylthio, or C1-6 aryl(C1-6) alkyloxy (e.g., phenyl(C1-6)alkyloxy and benzyl(C1-6)alkyloxy), and

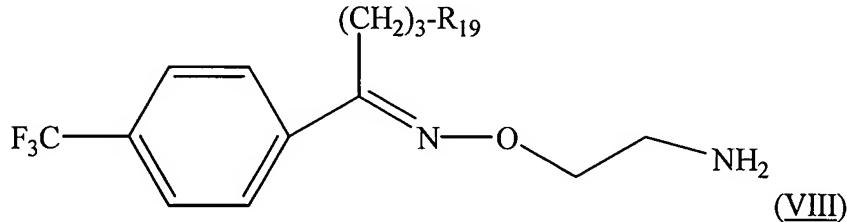
R_{15} represents an alkyl or alkynyl group having 1-4 carbon atoms, or a phenyl group optionally substituted by C1-4 alkyl, C1-6 alkylthio, C1-6 alkoxy, halogen, nitro, acylamino, methylsulfonyl or methylenedioxy, or represents tetrahydronaphthyl.

12. The preparation of claim 5, wherein the SSRI is a compound having a structure represented in formula (VII), or a pharmaceutically acceptable salts thereof:



wherein R₁₆ and R₁₇ are each independently represent a halogen, a trifluoromethyl group, a cyano group or -C(=O)-R₁₈, wherein R₁₈ is an alkyl radical with from 1-4 C-atoms inclusive.

13. The preparation of claim 5, wherein the SSRI is a compound having a structure represented in formula (VIII), or a pharmaceutically acceptable salts thereof:



wherein R₁₉ represents a cyano group, a cyanomethyl group, a methoxymethyl group or an ethoxymethyl group.

14. The preparation of claim 1, formulated for oral administration.
15. The preparation of claim 1, wherein the nefazodonoid and SRI are commingled in single dosage form.
16. The preparation of claim 1, wherein the nefazodonoid and SRI are provided in separate dosage form.

- Q.3
17. The preparation of any of claims 1-16, wherein the nefazonoid is provided in an amount, for single dosage, to reach the ED₅₀ for 5-HT receptor inhibition, but less than half the ED₅₀ for inhibition of serotonin reuptake.
 18. The preparation of claim 17, wherein the SRI is provided in an amount, for single dosage, to reach the ED₅₀ for inhibition of serotonin reuptake, but less than half the ED₅₀ for 5-HT receptor inhibition.
 19. A pharmaceutical preparation comprising, in a single dosage form, a mixture of a nefazodonoid and a fluoxetinoid.
 20. The pharmaceutical preparation of claim 19, wherein the nefazodonoid is selected from nefazodone, hydroxynefazodone, oxonefazodone, a mixture thereof, and pharmaceutically acceptable salts thereof.
 21. The pharmaceutical preparation of claim 20, wherein the single dosage form contains from 10-100 mg nefazodone, hydroxynefazodone or oxonefazodone.
 22. The pharmaceutical preparation of claim 20, wherein the single dosage form contains less than 50 mg nefazodone, hydroxynefazodone or oxonefazodone.
 23. The pharmaceutical preparation of claim 19, wherein the single dosage form contains from 5-40 mg fluoxetine or norfluoxetine.
 24. The pharmaceutical preparation of claim 19, wherein the single dosage form contains, less than) 20 mg fluoxetine and norfluoxetine.
 25. A kit comprising
 - a. in single dosage form, a nefazodonoid and a selective serotonin reuptake inhibitor, each in a pharmaceutically acceptable excipient;

b. instructions for co-administering the nefazodonoid and a selective serotonin reuptake inhibitor in a treatment of a serotonin-mediated disorder.

26.

A method for treating a 5-HT receptor-mediated disorder in an animal, comprising co-administering to the animal

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an amount of a nefazodonoid sufficient to inhibit a 5-HT₂ receptor activity to a therapeutically effective extent, and

an amount of a serotonin reuptake inhibitor (SRI) sufficient to inhibit serotonin reuptake to a therapeutically effective extent, wherein the nefazodonoid is administered at a dosage below the necessary dosage to inhibit serotonin reuptake to a therapeutically effective extent in the absence of the SRI.

27.

The method of claim 26, wherein the nefazodonoid and the SRI are administered simultaneously.

28.

The method of claim 27, wherein the nefazodonoid and the SRI are administered as part of a single composition.

29.

The method of claim 28, wherein the single composition is for oral administration.

30.

The method of claim 26, wherein the nefazodonoid is selected from nefazodone, hydroxynefazodone, oxonefazodone, a mixture thereof, and pharmaceutically acceptable salts thereof.

31.

The method of claim 30, wherein the nefazodonoid is R-hydroxynefazodone.

32.

The method of claim 26, 30 or 31, wherein the SRI is a fluoxetinoid.

33. The method of claim 32, wherein the fluoxetinoid is selected from fluoxetine and norfluoxetine, a mixture thereof, and pharmaceutically acceptable salts thereof.
34. The method of claim 32, wherein the SSRI is R-fluoxetine.
35. A method for treating depression in a human patient, comprising administering to the patient (a) a nefazodonoid selected from nefazodone, hydroxynefazodone, or oxonefazodone in an amount of 100 mg or less per day, and (b) a fluoxetinoid selected from fluoxetine or norfluoxetine in an amount sufficient to inhibit serotonin reuptake to a therapeutically effective extent.
36. The method of claim 35, wherein the nefazodonoid and the fluoxetinoid are administered to the patient simultaneously.
37. The method of claim 35, wherein the fluoxetinoid is administered at a rate of 5-40 mg per day.
38. The method of claim 35, wherein the nefazodonoid is administered at a rate of less than 50 mg per day.
39. A method for preparing a pharmaceutical preparation, comprising combining a nefazodonoid, a fluoxetinoid, and a pharmaceutically acceptable excipient in a composition for simultaneous administration of the nefazodonoid and the fluoxetinoid.
- fails to properly define invention*
40. A pharmaceutical preparation of a nefazodonoid and a fluoxetinoid for use in the treatment of a 5-HT receptor mediated disorder.
41. A method for conducting a pharmaceutical business, comprising:
- manufacturing a preparation of claim 1 or a kit of claim 25; and

- b. marketing to healthcare providers the benefits of using the preparation or kit in the treatment of 5-HT receptor-mediated disorders.
- 42. A method for conducting a pharmaceutical business, comprising:
 - a. providing a distribution network for selling the preparation of claim 1 or the kit of claim 25; and
 - b. providing instruction material to patients or physicians for using the preparation to treat 5-HT receptor-mediated disorders.
- 43. A method for conducting a pharmaceutical business, comprising:
 - a. determining an appropriate formulation and dosage of a nefazodonoid and a selective serotonin reuptake inhibitor to be co-administered in the treatment of a 5-HT receptor mediated disorder;
 - b. conducting therapeutic profiling of formulations identified in step (a), for efficacy and toxicity in animals; and
 - c. providing a distribution network for selling a preparation identified in step (b) as having an acceptable therapeutic profile.
- 44. The method of claim 43, including an additional step of providing a sales group for marketing the preparation to healthcare providers.
- 45. A method for conducting a pharmaceutical business, comprising:
 - a. determining an appropriate formulation and dosage of a nefazodonoid and a selective serotonin reuptake inhibitor to be co-administered in the treatment of a 5-HT receptor mediated disorder; and
 - b. licensing, to a third party, the rights for further development and sale of the formulation.
- 46. A single dosage formulation of having 10-50mg of nefazodone, hydroxynefazodone or oxonefazodone, or a mixture thereof.